

AMENDMENT

Please amend the application without prejudice, without admission, without surrender of subject matter and without intention of creating any estoppel as to equivalents, as follows.

In the Claims

1. (Cancelled)

2. (Currently amended) A modified monomeric non-antibody ligand V-like domain (VLD) comprising within the VLD at least one CDR loop structure or part thereof that is modified or replaced such that

- (i) the size of the CDR loop structure or part thereof is increased by at least one amino acid residue when compared with the corresponding CDR loop structure or part thereof in an unmodified VLD; and/or
- (ii) the modification or replacement results in formation of a disulphide bond within or between one or more of the CDR loop structures,

wherein the CDR loop structure is a surface polypeptide loop structure corresponding to a complementarity determining region of an antibody V-domain, and wherein the non-antibody ligand is selected from the group consisting of CTLA-4, CD28 and ICOS.

3. (Cancelled)
4. (Previously presented) The modified VLD according to claim 2, wherein the size of the CDR loop structure or part thereof is increased by at least two amino acid residues.
5. (Previously presented) The modified VLD according to claim 2, wherein the size of the CDR loop structure or part thereof is increased by at least six amino acid residues.
6. (Previously presented) The modified VLD according to claim 2, wherein the size of the CDR loop structure or part thereof is increased by at least nine amino acid residues.
7. (Previously presented) The modified VLD according to claim 2, wherein the binding affinity of the modified VLD is altered when compared with the unmodified VLD.
8. (Previously presented) The modified VLD according to claim 7, wherein the affinity of the modified VLD to at least one natural ligand of the unmodified VLD is reduced.
9. (Previously presented) The modified VLD according to claim 2, wherein the binding specificity of the modified VLD is different than that of the unmodified VLD.
10. (Cancelled)
11. (Cancelled)

12. (Previously presented) The modified VLD according to claim 2, wherein the non-antibody ligand is CTLA-4.

13. (Previously presented) The modified VLD according to claim 2, wherein one or more of the CDR loop structure(s) or part(s) thereof is replaced with a binding determinant derived from a non-antibody polypeptide.

14. (Previously presented) The modified VLD according to claim 13, wherein the binding determinant is derived from somatostatin or haemagglutinin.

15. (Previously presented) The modified VLD according to claim 2, wherein one or more of the CDR loop structure(s) or parts thereof is replaced with one or more CDR loop structures derived from an antibody or antibodies.

16. (Previously presented) The modified VLD according to claim 15, wherein the antibody or antibodies are derived from a rat, mouse, human, camel, llama or shark.

17. (Previously presented) The modified VLD according to claim 15, wherein the antibody or antibodies are selected from the camel antibody cAB-Lys3 and the human anti-melanoma antibody V86.

18. (Previously presented) The modified VLD according to claim 2, linked to a diagnostic reagent.

19. (Previously presented) The modified VLD according to claim 18, wherein the diagnostic reagent is selected from the group consisting of streptavidin, biotin, a radioisotope, a dye marker and an imaging reagent.

20. (Previously presented) A multivalent reagent comprising two or more modified VLDs as claimed in claim 2.

21. (Currently amended) The modified VLD ~~or multivalent reagent~~ according to claim 2, immobilized ~~or 20, immobilised~~ on a solid support or coupled to a biosensor surface.

22-27. (Cancelled)

28. (Currently amended) A composition in a pharmaceutically acceptable carrier or diluent comprising a modified VLD ~~or multivalent reagent~~ as claimed in claim 2 ~~or 20~~.

29-33. (Cancelled)

34. (Previously presented) The modified VLD according to claim 2, wherein at least two CDR loop structures or parts thereof are modified or replaced.

35. (Previously presented) The modified VLD according to claim 2, wherein three CDR loop structures or parts thereof are modified or replaced.

36. (Cancelled)

37. (Cancelled)

38. (Previously presented) The modified monomeric VLD according to claim 2, wherein the solubility of the modified VLD is improved when compared with the unmodified VLD.

39-41. (Cancelled)

42. (New) The multivalent reagent according to claim 20, immobilized on a solid support or coupled to a biosensor surface.

43. (New) A composition in a pharmaceutically acceptable carrier or diluent comprising multivalent reagent as claimed in claim 20.